Appl. No. 10/699,562 Amdt. dated August 13, 2007 Amendment under 37 CFR 1.116 Expedited Procedure Examining Group 1618

Listing of the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

2

D-amino acids

1 1 (previously presented): A molecule of the structure A - X - B, wherein 2 B is a peptide portion of about 5 to about 20 basic amino acid residues, which is 3 suitable for cellular uptake. 4 A is a peptide portion of about 2 to about 20 acidic amino acid residues, which 5 when linked with portion B is effective to inhibit or prevent cellular uptake of portion B, and 6 X is a linker of about 2 to about 100 atoms joining A with B, which can be 7 cleaved under physiological conditions, wherein X comprises the sequence of SEO ID NO: 1. 1 2 (original): The molecule of claim 1, wherein said peptide portion A comprises 2 about 5 to about 9 glutamates or aspartates. 1 3 (original): The molecule of claim 2, wherein said peptide portion A comprises 2 about 5 to about 9 consecutive glutamates or aspartates. 1 4 (original): The molecule of claim 1, wherein said peptide portion B comprises 2 about 9 to about 16 arginines. 1 5 (original): The molecule of claim 4, wherein said peptide portion B comprises 2 about 9 to about 16 consecutive arginines. 1 6 (original): The molecule of claim 1, wherein said peptide portion A comprises 2 D-amino acids. 1 7 (original): The molecule of claim 1, wherein said peptide portion B comprises

Appl. No. 10/699,562 Amdt. dated August 13, 2007 Reply to Office Action of June 14, 2007

1

2

1	8 (original): The molecule of claim 1, wherein said peptide portion A consists of
2	D-amino acids.
1	9 (original): The molecule of claim 1, wherein said peptide portion B consists of
2	D-amino acids.
l	10 (original): The molecule of claim 1, wherein said peptide portions A and B
2	consists of D-amino acids.
1	11 (previously presented): A molecule for transporting a cargo moiety across a
2	cell membrane of the structure $A - X - B - C$, wherein
3	C is a portion comprising a cargo moiety,
4	B is a peptide portion of about 5 to about 20 basic amino acid residues, which is
5	suitable for cellular uptake, is covalently linked to portion C, and is effective to enhance
6	transport of cargo portion C across a cell membrane,
7	A is a peptide portion of about 2 to about 20 acidic amino acid residues, which
8	when linked with portion B is effective to inhibit or prevent cellular uptake of B - C , and
9	X is a cleavable linker of about 2 to about 100 atoms joining A with B-C, which
10	can be cleaved under physiological conditions, wherein X comprises the sequence of SEQ ID
11	NO: <u>1</u> .
1	12 (original): The molecule of claim 11, wherein said peptide portion A
2	comprises amino acids selected from the group of acidic amino acids consisting of glutamate and
3	aspartate.
1	13 (original): The molecule of claim 11, wherein said peptide portion B
2	comprises amino acids selected from the group of basic amino acids consisting of arginine and
3	histidine.

from the group of cargo moieties consisting of a fluorescent moiety, a fluorescence-quenching

14 (original): The molecule of claim 11, wherein said cargo portion C is selected

3 4

5

- moiety, a radioactive moiety, a radiopaque moiety, a paramagnetic moiety, a nanoparticle, a vesicle, a molecular beacon, a marker, a marker enzyme, a contrast agent, a chemotherapeutic agent, and a radiation-sensitizer.
- 15 (original): The molecule of claim 14, wherein the cargo portion C comprises
 a contrast agent for diagnostic imaging.
- 16 (original): The molecule of claim 14, wherein the cargo portion C comprises
 a radiation sensitizer for radiation therapy.
- 1 17 (original): The molecule of claim 11, wherein said peptide portion A
 2 comprises about 5 to about 9 glutamates or aspartates.
- 1 18 (original): The molecule of claim 17, wherein said peptide portion A
 2 comprises about 5 to about 9 consecutive glutamates or aspartates.
- 19 (original): The molecule of claim 11, wherein said portion peptide B
 comprises between about 9 to about 16 arginines.
- 1 20 (original): The molecule of claim 19, wherein said peptide portion **B** comprises between about 9 to about 16 consecutive arginines.
- 21 (original): The molecule of claim 11, wherein said peptide portion A
 comprises D-amino acids.
- 22 (original): The molecule of claim 11, wherein said peptide portion B
 comprises D-amino acids.
- 23 (original): The molecule of claim 11, wherein said peptide portion A consists
 of D-amino acids.
- 24 (original): The molecule of claim 11, wherein said peptide portion B consists
 of D-amino acids.

Appl. No. 10/699,562 Amdt. dated August 13, 2007 Reply to Office Action of June 14, 2007

1	25 (original): The molecule of claim 11, wherein said peptide portions A and B consist of D-amino acids.
1 2	26 (original): The molecule of claim 25, wherein said peptide portion B consists of D-arginine amino acids.
1 2	27 (original): The molecule of claim 11, wherein said peptide portion $\bf A$ is located at a terminus of a polypeptide chain comprising $\bf B-\bf C$.
1	28 (original): The molecule of claim 11, wherein said peptide portion $\bf A$ is located at the amino terminus of a polypeptide chain comprising $\bf B-\bf C$.
1 2	29 (original): The molecule of claim 11, wherein said peptide portion $\bf A$ is linked near to or at the amino terminus of a polypeptide chain comprising $\bf B-\bf C$.
1 2	30 (original): The molecule of claim 11, wherein said peptide portion $\bf A$ is linked near to or at the carboxy terminus of a polypeptide chain comprising $\bf B-\bf C$.
1 2 3	31 (original): The molecule of claim 11, wherein $\mathbf{B} - \mathbf{C}$ comprises a polypeptide chain having ends consisting of a \mathbf{B} -side terminus and a \mathbf{C} -side terminus, and wherein cleavable linker \mathbf{X} is disposed near or at said \mathbf{B} -side terminus.
1 2 3	32 (original): The molecule of claim 11, wherein $\mathbf{B} - \mathbf{C}$ comprises a polypeptide chain having ends consisting of a \mathbf{B} -side terminus and a \mathbf{C} -side terminus, and wherein cleavable linker \mathbf{X} is disposed near or at said \mathbf{C} -side terminus.
	33-36 (canceled)
1	37 (original): The molecule of claim 11, wherein cleavable linker X comprises aminocaproic acid.

Page 5 of 12

38-44 (canceled)

Appl. No. 10/699,562 Amdt. dated August 13, 2007 Reply to Office Action of June 14, 2007

1	45 (original): The molecule of claim 11, comprising a plurality of cleavable
2	linkers X linking a portion A to a structure $B - C$.
1	46 (previously presented): A pharmaceutical composition comprising:
2	A molecule of the structure $A - X - B$, wherein
3	B is a peptide portion of about 5 to about 20 basic amino acid residues, which is
4	suitable for cellular uptake,
5	A is a peptide portion of about 2 to about 20 acidic amino acid residues, which
6	when linked with portion B is effective to inhibit or prevent cellular uptake of portion B, and
7	
	X is a cleavable linker of about 3 to about 30 atoms joining A with B, which can
8	be cleaved under physiological conditions, wherein X comprises the sequence of SEQ ID NO: 1;
9	and
0	a pharmaceutically acceptable carrier.
1	47 (previously presented): The pharmaceutical composition of claim 46, wherein
2	said portion A has between about 5 to about 9 acidic amino acid residues, and said
3	portion B has between about 9 to about 16 basic amino acid residues.
1	48 (original): The pharmaceutical composition of claim 46 or 47, further
2	comprising a portion C covalently attached to said portion B and comprising a cargo moiety.
1	49 (withdrawn): A method of modulating cellular uptake of a peptide B of about
2	5 to about 20 basic amino acid residues, which is suitable for cellular uptake, comprising:
3	linking said peptide B to a peptide A of about 2 to about 20 acidic amino acid
4	residues with a cleavable linker X of about 3 to about 30 atoms, which can be cleaved under
5	physiological conditions and
6	cleaving said cleavable linker X effective to separate peptide B from molecule A .
1	50 (withdrawn): A method of modulating cellular uptake of a cargo moiety C,
2	comprising:

3	covalently attacking a caree mainty City a most in B. S. L. 15 (1)
4	covalently attaching a cargo moiety C to a peptide B of about 5 to about 20 basic
	amino acid residues to form a molecule B – C ;
5	linking said molecule B - C to a peptide A of about 2 to about 20 acidic amino
6	acid residues with a cleavable linker X of about 3 to about 30 atoms, and
7	cleaving said cleavable linker ${\bf X}$ effective to separate ${\bf B}-{\bf C}$ from said peptide ${\bf A}$.
1	51 (withdrawn): A nucleic acid encoding a molecule of the structure $\mathbf{A} - \mathbf{X} - \mathbf{B}$,
2	wherein
3	B is a peptide of about 5 to about 20 basic amino acid residues, which is suitable
4	for cellular uptake,
5	A is a peptide of about 2 to about 20 acidic amino acid residues; which when
6	linked with peptide ${\bf B}$ is effective to inhibit or prevent cellular uptake of peptide ${\bf B}$, and
7	X is a cleavable linker portion of between 1 and 10 amino acid residues joining A
8	with B, which can be cleaved under physiological conditions.
1	52 (withdrawn): A nucleic acid encoding a molecule of the structure $\mathbf{A} - \mathbf{X} - \mathbf{B} -$
1 2	52 (with drawn): A nucleic acid encoding a molecule of the structure ${\bf A}-{\bf X}-{\bf B}-{\bf C},$ wherein
	•
2	C, wherein
2	C, wherein C is a peptide cargo moiety,
2 3 4	C, wherein C is a peptide cargo moiety, B is a peptide of about 5 to about 20 basic amino acid residues, which is suitable
2 3 4 5	C, wherein C is a peptide cargo moiety, B is a peptide of about 5 to about 20 basic amino acid residues, which is suitable for cellular uptake,
2 3 4 5 6	C, wherein C is a peptide cargo moiety, B is a peptide of about 5 to about 20 basic amino acid residues, which is suitable for cellular uptake, A is a peptide of about 2 to about 20 acidic amino acid residues, which when
2 3 4 5 6 7	C, wherein C is a peptide cargo moiety, B is a peptide of about 5 to about 20 basic amino acid residues, which is suitable for cellular uptake, A is a peptide of about 2 to about 20 acidic amino acid residues, which when linked with peptide B is effective to inhibit or prevent cellular uptake of peptide B - C, and
2 3 4 5 6 7 8	C, wherein C is a peptide cargo moiety, B is a peptide of about 5 to about 20 basic amino acid residues, which is suitable for cellular uptake, A is a peptide of about 2 to about 20 acidic amino acid residues, which when linked with peptide B is effective to inhibit or prevent cellular uptake of peptide B - C, and X is a cleavable linker portion of between 1 and 10 amino acid residues joining A with B - C which can be cleaved under physiological conditions. 53 (withdrawn): A molecule for transporting a fluorescent cargo moiety across a
2 3 4 5 6 7 8 9	C, wherein C is a peptide cargo moiety, B is a peptide of about 5 to about 20 basic amino acid residues, which is suitable for cellular uptake, A is a peptide of about 2 to about 20 acidic amino acid residues, which when linked with peptide B is effective to inhibit or prevent cellular uptake of peptide B - C, and X is a cleavable linker portion of between 1 and 10 amino acid residues joining A with B - C which can be cleaved under physiological conditions.

Appl. No. 10/699,562 Amdt, dated August 13, 2007 Reply to Office Action of June 14, 2007

7

8

9

10

11

12

1

4 B is a peptide portion of about 5 to about 20 basic amino acid residues, which is suitable for cellular uptake, is covalently linked to portion C, and is effective to enhance 5 6 transport of cargo portion C across a cell membrane,

Q is a quencher moiety attached to A and effective to quench fluorescence from fluorescent cargo C;

when linked with portion \mathbf{B} is effective to inhibit or prevent cellular uptake of $\mathbf{B} - \mathbf{C}$, and X is a cleavable linker of about 2 to about 100 atoms joining A with B - C, which can be cleaved under physiological conditions.

A is a peptide portion of about 2 to about 20 acidic amino acid residues, which

54-55 (canceled)

56 (original): The molecule of claim 11, comprising a single cargo portion C 2 linked to a plurality of portions B, each of portions B being linked to a cleavable linker portion X 3 linked to an acidic portion A.